Claims

1. An isolated antibody capable of binding an extracellular Aspergillus fumigatus polypeptide selected from the group consisting of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), and catalase A (SEQ ID NO:6).

2. The antibody of claim 1, wherein the antibody binds said polypeptide with a dissociation constant of less than 10^{-7}M, e.g. less than 5 X 10^{-8}M, such as less than 10^{-8}M, e.g. less than 5 X 10^{-9}M, such as less than 10^{-9}M, e.g. less than 5 X 10^{-10}M, such as less than 10^{-10}M, e.g. less than 5 X 10^{-11}M, such as less than 10^{-11}M, e.g. less than 5 X 10^{-12}M, such as less than 10^{-12}M, e.g. less than 5 X 10^{-13}M, such as less than 10^{-13}M, e.g. less than 5 X 10^{-14}M, such as less than 10^{-14}M, e.g. less than 5 X 10^{-15}M, or less than 10^{-15}M.

3. The antibody of any of the preceding claims, wherein the antibody is selected from the group consisting of IgG, IgA, IgE, IgM and IgD, wherein IgG preferably is IgG1.

4. The antibody of any of the preceding claims, wherein the antibody is capable of binding an intact Aspergillus fumigatus cell.

5. The antibody of any of the preceding claims, wherein the antibody, or at least an Fab fragment thereof, is capable of reducing the adhesion of Aspergillus fumigatus conidia to lung epithelia in an in vitro assay, preferably reducing said adhesion with at least 20%, e.g. at least 40%, or at least 60%.

6. The antibody of any of the preceding claims, wherein the antibody or at least an Fab fragment thereof, is capable of reducing the germination of Aspergillus fumigatus conidia in an in vitro assay, preferably reducing said adhesion with at least 20%, e.g. at least 40%, or at least 60%.

7. The antibody of any of claims 1-6, wherein the antibody is polyclonal.

8. The antibody of any of claims 1-6, wherein the antibody is monoclonal.

9. The antibody of claim 8, wherein the antibody is a chimeric, human or humanised antibody.

10. The antibody of claim 8, wherein the antibody is a human antibody.

11. The antibody of any of the preceding claims, wherein the antibody is purified.

12. The antibody of any of the preceding claims, wherein the antibody is further capable of binding a homologous polypeptide, wherein the homologous polypeptide has a sequence identity of 39% or more, such as 42% or more, e.g. 48% or more, such as 68% or more, e.g. 80% or more, such as 90% or more, to a polypeptide selected from the group consisting of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), and catalase A (SEQ ID NO:6).

13. The antibody of claim 12, wherein said homologous polypeptide originates from

- an Aspergillus species, such as Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger, or Aspergillus oryzea,
- Neurospora crassa,
- Saccharomyces cerevisiae,
- a Candida species such as Candida albicans,
- a Coccidioides species, such as Coccidioides posadasii, or Coccidioides immitis,
- a Cryptococcus species, such as Cryptococcus neoformans var. neoformans,
- a Fusarium species,
- a Pneumocystis species,
- a Penicillium species,

or

- Histoplasma capsulatum.

14. The antibody of claim 13, wherein said homologous polypeptide originates from

- an Aspergillus species, such as Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger or Aspergillus oryzea,
- Candida albicans,
- Coccidioides posadasii,

or

- Cryptococcus neoformans var. neoformans.

15. The antibody of claim 14, wherein said homologous polypeptide originates from an Aspergillus species, such as Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger or Aspergillus oryzea.

16. The antibody of claim 15, wherein said homologous polypeptide originates from Aspergillus fumigatus.

17. The antibody of claim 16, wherein the said homologous polypeptide is the polypeptide of SEQ ID NO:41.

18. The antibody of any of claims 12-17, wherein said homologous polypeptide is extracellular.

19. The antibody of any of the preceding claims, wherein the antibody further is capable of binding an intact cell of any one or more of

- an Aspergillus species other than Aspergillus fumigatus, such as Aspergillus nidulans, Aspergillus niger, or Aspergillus oryzea,
- Neurospora crassa,
- Saccharomyces cerevisiae,
- a Candida species such as Candida albicans,
- a Coccidioides species, such as Coccidioides posadasii, or Coccidioides immitis,
- a Cryptococcus species, such as Cryptococcus neoformans var. neoformans,
- a Fusarium species,
- a Pneumocystis species,
- a Penicillium species,

or

- Histoplasma capsulatum.

20. The antibody of any of claims 1-11, wherein the antibody is not capable of binding an intact cell of any of

- Neurospora crassa,
- Saccharomyces cerevisiae,
- Candida albicans,
- Coccidioides posadasii, or Coccidioides immitis,

- Cryptococcus neoformans var. neoformans,

or

- Histoplasma capsulatum.

21. The antibody of any of the preceding claims, wherein the antibody is capable of binding a polypeptide selected from the group consisting of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1) and catalase A (SEQ ID NO:6).

22. The antibody of any of the preceding claims, wherein the antibody is capable of binding a polypeptide selected from the group consisting of isopropylmalate dehydrogenase B (SEQ ID NO:36) and CssI (SEQ ID NO:1).

23. The antibody of any of the preceding claims, wherein the antibody is capable of binding isopropylmalate dehydrogenase B (SEQ ID NO:36).

24. The antibody of claim 23, wherein the antibody is capable of binding an epitope which comprises one or more of the residues of a region of SEQ ID NO:36 selected from the group consisting of: Ser67- Leu71, Ala74-Trp80, Ser191-Arg205, Leu268-Leu273, His292-Pro296, Glu355-Ile360, Asp193-Glu209, Asp193-Ala199, Ile15-Val19, Val75-Trp80, Pro11-Glu18 and the region defined by SEQ ID NO:37, preferably an epitope which is entirely consisting of residues comprised within said region.

25. A pharmaceutical composition comprising an antibody as defined in any of claims 1-24 and a pharmaceutically-acceptable carrier.

26. An antibody as defined in any of claims 1-24 or a composition as defined in claim 25 for use as a medicament.

27. Use of an antibody as defined in any of claims 1-24 or a composition as defined in claim 25 for the manufacture of a medicament for the treatment or prevention of fungal infections.

28. Use of claim 27, wherein the medicament is a medicament for the treatment or prevention of Aspergillus infections, preferably Aspergillus fumigatus infections.

29. Use of claim 27, wherein the medicament is a medicament for the treatment or prevention of a fungal disease selected from the group consisting of: invasive

aspergillosis, aspergilloma, and allergic aspergillosis, such as allergic bronchopulmonary aspergillosis.

30. A composition comprising one or more Aspergillus fumigatus polypeptides selected from the group of:

polypeptides comprising SEQ ID NO:36, fragments thereof and variants thereof, fragments of SEQ ID NO:1 of less than 259 amino-acid residues in length, such as less than 200, preferably less than 150, such as less than 100, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:7,8,17,26,28,29 and/or 30 and variants of said fragments;

fragments of SEQ ID NO:2 of less than 106 amino-acid residues in length, such as less than 75, preferably less than 50, such as less than 25 residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:9,10,18 and/or 19 and variants of said fragments;

polypeptides comprising SEQ ID NO:3, fragments thereof and variants thereof, with the proviso that if the polypeptide is a fragment of SEQ ID NO:3, that this fragment is not the fragment set forth in SEQ ID NO:35;

fragments of SEQ ID NO:4 of less than 437 amino-acid residues in length, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:13,14,23,24 and/or 25 and variants of said fragments;

fragments of SEQ ID NO:5 of less than 727 amino-acid residues in length, e.g. less than 400, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:15,16 and/or 27 and variants of said fragments; and

fragments of SEQ ID NO:6 of less than 748 amino-acid residues in length, e.g. less than 400, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:34 and variants of said fragments.

31. An *Aspergillus fumigatus* polypeptide selected from the group of:

polypeptides comprising SEQ ID NO:36, fragments thereof and variants thereof, fragments of SEQ ID NO:1 of less than 259 amino-acid residues in length, such as less than 200, preferably less than 150, such as less than 100, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:7,8,17,26,28,29 and/or 30 and variants of said fragments;

fragments of SEQ ID NO:2 of less than 106 amino-acid residues in length, such as less than 75, preferably less than 50, such as less than 25 residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:9,10,18 and/or 19 and variants of said fragments;

polypeptides comprising SEQ ID NO:3, fragments thereof and variants thereof, with the proviso that if the polypeptide is a fragment of SEQ ID NO:3, that this fragment is not the fragment set forth in SEQ ID NO:35;

fragments of SEQ ID NO:4 of less than 437 amino-acid residues in length, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:13,14,23,24 and/or 25 and variants of said fragments;

fragments of SEQ ID NO:5 of less than 727 amino-acid residues in length, e.g. less than 400, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:15,16 and/or 27 and variants of said fragments; and

fragments of SEQ ID NO:6 of less than 748 amino-acid residues in length, e.g. less than 400, such as less than 200, preferably less than 100, such as less than 75, e.g. less than 50, such as less than 25 amino-acid residues in length comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO:34 and variants of said fragments.

32. The polypeptide of claim31, wherein the polypeptide is a fragment comprising one or more residues of the amino-acid sequences set forth in SEQ ID NOs: 7-27 and/or 37, or a variant of said fragment.

33. The polypeptide of claim 32, wherein the polypeptide is a fragment comprising one or more residues of the amino-acid sequences set forth in SEQ ID NOs: 7-16, or a variant of said fragment.

34. The polypeptide of claim 32, wherein the polypeptide is a fragment comprising one or more residues of the amino-acid sequences set forth in SEQ ID NOs: 17-25 and/or SEQ ID NO:14, or a variant of said fragment.

35. The polypeptide of claim 32, wherein the polypeptide is a fragment comprising one or more residues of the amino-acid sequences set forth in SEQ ID NO: 18, 19, 26, 27, and/or 37, or a variant of said fragment.

36. A polynucleotide encoding a polypeptide as defined in any of claims 31-35.

37. An expression vector comprising a polynucleotide as defined in claim 36.

38. A host cell transformed or transfected with a polynucleotide as defined in claim 36 and/or an expression vector as defined in claim 37.

39. A pharmaceutical composition comprising a polypeptide as defined in any of claims 31-35 or a polynucleotide as defined in claim 36 and a pharmaceutically-acceptable carrier.

40. A polypeptide as defined in any of claims 31-35, or a polynucleotide as defined in claim 36 for use as a medicament.

41. Use of a polypeptide as defined in any of claims 31-35, a polynucleotide as defined in claim 36 for the manufacture of a medicament for the immunisation of a mammal against fungal infections.

42. The use of claim 41, wherein said mammal is a human being.

43. A method for raising specific antibodies to a polypeptide selected from the group of polypeptides set forth in SEQ ID NO:1, 2, 3, 6 and 36 in a non-human mammal comprising the steps of:

a. providing a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2),

GAPDH (SEQ ID NO:3), and catalase A (SEQ ID NO:6), or a polypeptide as defined in any of claims 31-35, or a cell expressing any of these polypeptides,

b. introducing a composition comprising said polypeptide or said cell into said animal,

c. raising antibodies in said animal, and

d. isolating and optionally purifying the antibodies.

44. The method of claim 43, wherein the raising of antibodies is done in a transgenic animal which is capable of producing human antibodies.

45. The method of claim 43 or 44, wherein the polypeptide that is provided is isopropylmalate dehydrogenase B (SEQ ID NO:36) or a fragment thereof, or a variant of said polypeptide.

46. The method of claim 43 or 44, wherein the polypeptide that is provided is CssI (SEQ ID NO:1) or a fragment thereof, or a variant of said polypeptide.

47. The method of claim 43 or 44, wherein the polypeptide that is provided is hydrophobin (SEQ ID NO:2) or a fragment thereof, or a variant of said polypeptide.

48. The method of claim 43 or 44, wherein the polypeptide that is provided is GAPDH-B (SEQ ID NO:3) or a fragment thereof, or a variant of said polypeptide.

49. The method of claim 43 or 44, wherein the polypeptide that is provided is catalase A (SEQ ID NO:6) or a fragment thereof, or a variant of said polypeptide.

50. A method for identifying a binding partner of a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), enolase (SEQ ID NO:4), catalase B (SEQ ID NO:5) and catalase A (SEQ ID NO:6), comprising the steps of :

a. providing a polypeptide as defined in any of claims 31-35 or a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), catalase B (SEQ ID NO:5), and catalase A (SEQ ID NO:6),

b. contacting said polypeptide with a putative binding partner, and

c. determining whether said putative binding partner is capable of binding to said polypeptide.

51. The method of claim 50, wherein the putative binding partner is a host-derived molecule.

52. The method of any of claims 50-51, wherein said method is repeated for a plurality of putative binding partners.

53. A method for identifying a compound with antifungal activity comprising the steps of:

a. providing a sensitised cell which has a reduced level of a polypeptide selected from the group of SEQ ID NOs:1,2,3,5,6, and 36 and

b. determining the sensitivity of said cell to a putative antifungal compound, for instance by a growth assay.

54. A method for identifying an inhibitor of an extracellular *Aspergillus* polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), GAPDH (SEQ ID NO:3), and catalase A (SEQ ID NO:6), comprising the steps of:

a. providing two cells which differ in the level of a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), GAPDH (SEQ ID NO:3), and catalase A (SEQ ID NO:6),

b. determining the sensitivity of said cells to a putative inhibitor, for instance by a growth assay, and

c. determining whether said two cells are differently affected by the presence of said putative inhibitor.

55. The method of claim 54, wherein the two cells differ in the copy number of said polypeptide.

56. The method of claim 54, wherein the two cells differ in the activity of said polypeptide.

57. A method of diagnosing fungal, preferably Aspergillus fumigatus, infection comprising the steps of:

a. providing a sample from an individual,

b. contacting said sample with an indicator moiety capable of specifically recognising and binding a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), and catalase A (SEQ ID NO:6), and

c. determining whether a signal has been generated by the indicator moiety.

58. The method of the preceding claim, wherein said indicator moiety is or comprises an antibody, such as an antibody as defined in any of claims 1-24.

59. A kit for the detection of fungal material, preferably intact fungal cells, most preferably intact Aspergillus fumigatus cells, in a biological sample comprising:

a. an indicator moiety capable of specifically recognising and binding a polypeptide selected from the group of isopropylmalate dehydrogenase B (SEQ ID NO:36), CssI (SEQ ID NO:1), hydrophobin (SEQ ID NO:2), GAPDH-B (SEQ ID NO:3), and catalase A (SEQ ID NO:6), and

b. one or more of: a buffer for promoting binding of the indicator moiety to the fungal material; a reagent for generating a detectable signal; and written instructions to the user.

60. The kit of claim 59, wherein said indicator is or comprises an antibody, such as an antibody as defined in any of claims 1-24.